510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

k121752

B. Purpose for Submission:

New Device

C. Measurand:

Hemoglobin

D. Type of Test:

Quantitative

E. Applicant:

MEC Dynamics Corporation (MEC)

F. Proprietary and Established Names:

Avie™ Total Hb Test System

G. Regulatory Information:

1. Regulation section:

   21 CFR §864.5620, Automated hemoglobin system

2. Classification:

   Class II

3. Product code:

   GKR, System, hemoglobin, automated

4. Panel:

   Hematology (81)

H. Intended Use:

1. Intended use(s):

   The Avie™ Total Hb Test System is for the quantitative measurement of total hemoglobin in whole blood (capillary or venous EDTA, K2). The test system is designed for point-of-care use in primary care settings. The test system is for professional *in vitro* diagnostic use only.

2. Indication(s) for use:

   Same as intended use

3. Special conditions for use statement(s):

   For prescription use

4. Special instrument requirements:

   Avie™ Total Hb Test strips are only to be used with Avie™ Total Hb Reader.

I. Device Description:

The Avie™ Total Hemoglobin Test is a point of care (POC) IVD system that utilizes general chemistry reactions to quantify total hemoglobin in fresh capillary blood and venous blood. The test system includes a small instrument (Reader) and disposable reagent strips. The reagent strips are packaged in a reusable canister with desiccant.

The Reader is a simple device containing electronics and optics for locating strip placement and sample detection. The device utilizes a power button and a LCD display with a molded plastic housing. The Reader is light-weight, weighing approximately one pound and it measures 1 ¾" high x 5½" long x 3¾" wide.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   HemoCue® 201+ System

2. Predicate 510(k) number(s):

   k041234

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	The Avie™ Total Hb Test System is for the quantitative measurement of total hemoglobin in whole blood (capillary or venous EDTA, K2). The test system is designed for point-of-care use in primary care settings. This test system is for professional in vitro diagnostic use only.	Quantitative determination of hemoglobin in capillary, venous, and arterial whole blood. For in vitro diagnostic use.
Sample Type	Capillary and venous whole blood	Same
Visual Display	LCD readout	Same
Calibration	Factory calibrated reader against hemiglobincyanide (HiCN) method	Factory calibrated
Recommended Testing Environment	Doctors' offices	Same
Reagent Storage	Room temperature	Same

Differences		
Item	Device	Predicate
Test Principle	Photometric measurement of total hemoglobin concentration in sample	A modified azidemethohemoglobin reaction
Reaction time	15 sec	60 sec
Operating Conditions	59-113°F (15-45°C), less than 85% relative humidity (without condensation).	65-90°F (18-32°C), less than 85% relative humidity (without condensation).
Reportable Range	5- 24.0 g/dL	0- 25.6 g/dL
Quality Control Requirements	Users are directed to perform daily liquid control testing, testing of each new shipment and/or lot of test strips, or when test results are suspect	Users are directed to perform daily electronic quality control testing and liquid control testing: with each new shipment and/or lot of test strips, or when test results are suspect

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP17-A; Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.

CLSI EP5-A2; Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline Second edition

CLSI EP7-A2; Interference Testing in Clinical Chemistry; Approved Guideline- Second edition

CLSI C28 A3; Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline.

CLSI H15-A3; Reference and Selected Procedures for the Quantitative Determination of Hemoglobin in Blood; Approved Standard-Third Edition.

L. Test Principle:

The Avie™ Total Hemoglobin Test utilizes general chemistry reactions to quantify total hemoglobin in fresh capillary blood and venous blood. The reagent strip consists of two plastic parts (top and bottom) that "sandwich" the sample between the primary chemistry and other reaction components. The strip is designed to automatically drive the sequence of reactions in conjunction with the electronics. When the blood sample is applied to the test strip, an exact amount is automatically aspirated into the reaction well within the strip. In the reaction well, the blood sample is incubated and stabilized, and total hemoglobin is then quantified photometrically. The concentration of total hemoglobin is based on the optical intensity of the reaction within the quantitative area of the test strip.

M. Performance Characteristics:

1. Analytical performance:

   a. Precision/Reproducibility:

   Precision:

   An internal precision study was conducted according to CLSI EP5-A2 using three samples (low, middle, and high Hb levels). Frozen aliquots of each sample were thawed daily at room temperature and tested with Avie™ Hb test system. Each sample was tested twice in the morning and twice in the afternoon (4 replicates per day) by two operators for 20 days, to generate 80 results per level. For each sample, the %CVs was calculated for within-day and between-day (total) precision.

   All CV% values across all three samples were within the acceptable threshold value of ≤ 3% for within-run, between-run, between-day and total precision. Results are summarized below:

20-Day Precision Data Summary

Sample	N	Mean	Within-Run		Between-Run		Between-Day		Total	
		g/dL	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	80	6.69	0.10	1.3	0.07	0.9	0.15	1.9	0.19	2.5
Middle	80	15.70	0.18	1.2	0.16	1.0	0.33	2.1	0.41	2.6
High	80	20.09	0.12	0.6	0.18	0.9	0.14	0.7	0.26	1.3

An external precision study was conducted at 3 point-of-care sites. The study was performed with three levels of control materials that represented a low, middle and high total hemoglobin sample (i.e. targeted at 5.0 g/dL, 10.0 g/dL, and 14.0 g/dL). Each sample was tested three times a day (beginning, middle, and end of the test day), and a total of 19 different operators performed the testing using 4 Avie readers and 3 lots of test strips. Summarized combined results are presented in the table below:

Combined Sites POL Precision Data

Sample	N	x̄ g/dL	Within-run		Between-Run		Between-Day		Between-Operator		Between-Lot		Between-Site		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Level 1	90	5.4	0.11	2.0	0.11	2.0	0.12	2.1	0.10	1.8	0.00	0.1	0.12	2.2	0.11	2.1
Level-2	90	10.9	0.22	2.1	0.22	2.1	0.21	1.9	0.17	1.6	0.05	0.5	0.22	2.0	0.33	3.1
Level 3	90	14.1	0.30	2.2	0.30	2.2	0.28	2.0	0.26	1.9	0.09	0.7	0.31	2.2	0.37	2.6

All %CVs were within the acceptable threshold value of <5% and the means were in the assigned ranges as determined by the label value.

Reproducibility Study:

Reproducibility study was conducted at 3 physician's office laboratory (POL) sites with 2 operators per site. One (1) lot of test strips across sites and one (1) Avie™ Hb test reader per site using 3-levels of control. Each control was assayed 4 times per day for a minimum of 10 days over a 20-day period. All CV% values across the 3 study sites were within the acceptable threshold value of ≤5. Summarized results by site and combined sites are presented in the table below:

Site-1

Sample	N	Mean g/dL	Within Run		Between Run		Between Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	40	7.0	0.14	2.0	0.04	0.6	0.10	1.5	0.18	2.6
Mid	40	10.3	0.29	2.8	0.18	1.7	0.18	1.8	0.38	3.7
High	40	16.4	0.27	1.7	0.14	0.9	0.26	1.6	0.40	2.4

Site-2

Sample	N	Mean g/dL	Within Run		Between Run		Between Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	40	7.4	0.18	2.4	0.14	1.9	0.14	1.8	0.27	3.6
Mid	40	10.9	0.21	2.0	0.09	0.8	0.12	1.1	0.26	2.4
High	40	16.7	0.32	1.9	0.21	1.3	0.20	1.2	0.43	2.6

Site-3

Sample	N	Mean g/dL	Within Run		Between Run		Between Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	40	6.9	0.10	1.4	0.17	2.5	0.04	0.6	0.20	2.9
Mid	40	10.1	0.16	1.6	0.29	2.9	0.17	1.7	0.37	3.7
High	40	16.0	0.27	1.7	0.40	2.5	0.17	1.1	0.51	3.2

Combined sites

Sample	N	Mean g/dL	Within Run		Between Run		Between Day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	120	7.1	0.14	2.0	0.13	1.8	0.04	0.5	0.20	2.8
Mid	120	10.4	0.23	2.2	0.14	1.4	0.06	0.5	0.27	2.6
High	120	16.3	0.29	1.8	0.27	1.7	0.10	0.6	0.41	2.5

b. Linearity/assay reportable range:

Eleven samples that spanned a wide range of Hb concentrations were prepared by mixing various proportions of low and high concentration samples. Testing was performed in quadruplicate on one Avie™ test system with one lot of test strips. Observed results were compared to expected results, based on the mathematical calculations of the proportions. Acceptance criteria were based on recoveries that were within 10% of the expected values, and r^2 value from the linear regression should be ≥ 0.95. Linear regression was: y=1.0202x-0.1862, R^2=0.9953. Based on the data in this study, the Avie Total Hb Test System is linear between 4.9 and 24.3 g/dL, and the claimed range is 5 to 24 g/dL.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Calibration is traceable to hemiglobincyanide (HiCN) method.

Controls:

Commercial controls are recommended for use with the Avie™ Hb system. The controls are marketed under the name Eurotrol (New Jersey, USA), and were cleared under k963908.

Test Strip Stability:

Closed-vial stability was tested with two whole blood samples (one low and one high

Hb concentration) at specified time intervals (1, 2, 3 and 6 months) at 2-8°C, 25°C, 37°C and 45°C, and at 25°C for in-use stability. Stability results demonstrated an interim shelf life of 9 months when store at 2–8°C and at room temperature. Shelf life will be extended upon completion of real-time stability and meeting the predetermined acceptance criteria. Shipping stress study was performed using test strips stressed for 3 days at 37°C and then stored at 25°C and strips were also frozen and thawed for 5 days then stored at 25°C. Data demonstrated interim 9 months stability for Avie Total Test Strip when stored under these stressed conditions.

d. Detection limit:

See item M.1.b., linearity, above.

e. Analytical specificity:

Studies were performed to assess the effect of potential interferents on the Avie™ Total Hb Test System according to the CLSI EP7-A guideline. Ten (10) substances (biological and therapeutic) were prepared at noted concentrations, and three levels of whole blood sample (low, middle, and high levels Hb) were assayed for both neat (control) and with each substance (on-test) in sextuplicate by the Avie™ system. The on-test results were compared to the control results. For each interferent, the mean result, standard deviation (SD), and %CV were calculated for each set of replicates. The percent recovery was calculated for each sample for each interferent, and compared to its appropriate control without interferent. All observed differences were within the 10% specification for all substances across the Hb range. Results are summarized in the table below:

Results of Potential Interfering Substances Tested

Interferent (Tested conc.)	Sample	Control Avg.	Interferent Avg.	Std. Dev. (of Int)	% CV (of Int)	% Recovery
Acetaminophen **(20.0mg/dL)**	Low	8.1	8.1	0.14	1.75	100.2
	Med.	15.7	15.9	0.26	1.63	100.8
	High	22.2	22.3	0.22	0.97	100.5
Acetylsalicylic Acid **(5.0mg/dL)**	Low	7.7	8.0	0.23	2.90	103.9
	Med.	15.1	15.2	0.18	1.16	100.2
	High	21.7	21.5	0.46	2.13	99.2
L-Ascorbic Acid **(3.0mg/dL)**	Low	8.0	8.1	0.08	0.93	101.3
	Med.	15.7	15.7	0.12	0.74	100.2
	High	22.2	22.2	0.17	0.75	100.1
Bilirubin **(10.0mg/dL)**	Low	7.8	8.3	0.16	1.98	107.6
	Med.	15.0	16.1	0.17	1.05	106.1
	High	21.7	21.5	0.27	1.26	99.2
Creatinine **(5.0mg/dL)**	Low	8.1	8.1	0.05	0.68	99.8
	Med.	15.7	15.6	0.31	1.98	99.4
	High	22.2	22.2	0.22	1.00	100.3

Interferent (Tested conc.)	Sample	Control Avg.	Interferent Avg.	Std. Dev. (of Int)	% CV (of Int)	% Recovery
Ibuprofen **(50.0mg/dL)**	Low	7.6	7.8	0.31	3.97	102.2
	Med.	15.1	15.5	0.24	1.58	102.6
	High	21.6	22.0	0.36	1.65	101.8
Intralipid 20% **(400.0mg/dL)**	Low	7.8	8.6	0.12	1.41	109.8
	Med.	15.8	16.6	0.25	1.50	105.0
	High	22.4	22.5	0.14	0.63	100.5
Tetracycline HCl **(1.51mg/dL)**	Low	8.1	8.1	0.12	1.45	100.4
	Med.	15.5	15.6	0.13	0.81	100.6
	High	22.1	22.1	0.05	0.23	100.1
Urea **(257.0mg/dL)**	Low	8.1	8.2	0.10	1.29	100.4
	Med.	15.6	15.6	0.12	0.78	100.4
	High	22.2	22.1	0.10	0.47	99.8
Uric Acid **(23.5mg/dL)**	Low	7.7	8.2	0.15	1.79	106.7
	Med.	15.4	15.3	0.28	1.84	99.2
	High	22.4	22.7	0.25	1.10	101.1

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was performed at 3 U.S clinical sites including an internal study site to determine the correlation between the Avie™ Total Hb Test system, against both the HemoCue system and the reference HiCN method. Patient samples [capillary (fingerstick, FS) and venous blood (K2 EDTA)] were tested using 9 Avie™ Total Hb Readers and 4 test strip lots by staff who are typical of physician's office. Fifty to 85 subjects were enrolled at each site, a total of 185 volunteers were tested. The subjects included males (47%) and females (53%) within the age range of 18 year to 87 years. An additional 40 banked samples were altered for Hb concentrations at the extremes of the dynamic range, and were tested in order to assess performance at the lower and upper ends of the dynamic range (5 and 24 g/dL, respectively).
The acceptance criterion was defined as the correlation coefficient (r) ≥0.9 and slope was defined as 1.0 ±0.1. In addition, Allowable Total Error (ATE) boundaries for analytical testing for total hemoglobin were defined to be ± 7.0% of the reference method.

The summarized regression statistics are shown below for each of the four method comparisons.

POL ACCURACY DATA SUMMARY- Hb g/dL Avie (FS) vs HemoCue (FS)

Site #	n	Range (Avie™)	Regression Equation	"r"	CI* Slope	CI Intercept
1	84	8.9 to 18.0	y = 1.01x + 0.17	0.96	-0.81 to 1.15	0.94 to 1.08
2	50	9.8 to 15.5	y = 0.99x + 0.04	0.96	-1.12 to 1.21	0.91 to 1.08
3	50	9.4 to 18.8	y = 0.99x + 0.26	0.98	-0.53 to 1.05	0.93 to 1.04
Total	184	8.9 to 18.8	y = 1.03x - 0.25	0.97	-0.81 to 0.32	.99 to 1.07

*95% Confidence Interval

POL ACCURACY DATA SUMMARY-Hb g/dL Avie (FS) vs HiCN (FS)

Site #	n	Range	Regression Equation	"r"	CI* Slope	CI* Intercept
1	82	9.5 to 18.0	y = 1.03x - 0.41	0.97	-1.34 to 0.51	0.97 to 1.09
2	47	11.3 to 15.9	y = 1.06x - 1.02	0.97	-2.15 to 0.11	0.98 to 1.14
3	48	10.5 to 17.8	y = 1.04x - 0.53	0.97	-1.56 to 0.51	0.97 to 1.12
Total	177	9.5 to 18.0	y = 1.05x - 0.68	0.97	-1.22 to -0.15	1.01 to 1.09

POL ACCURACY DATA SUMMARY- Hb g/dL Avie (venous) vs HemoCue (venous)

Site #	n	Range	Regression Equation	"r"	CI Slope	CI Intercept
1	124	5.1 to 23.5	y = 1.02x + 0.03	0.99	-0.36 to 0.43	0.99 to 1.05
2	50	10.8 to 16.5	y = 1.04x + 0.12	0.96	-1.11 to 1.34	0.95 to 1.13
3	50	10.2 to 18.3	y = 1.07x - 0.57	0.97	-1.66 to 0.52	0.99 to 1.15
Total	224	5.1 to 23.5	y = 1.02x + 0.13	0.99	-0.2 to 0.46	1.00 to 1.04

POL ACCURACY DATA SUMMARY- g/dL Avie (venous) vs HiCN (venous)

Site #	n	Range	Regression Equation	"r"	CI* Slope	CI Intercept
1	124	5.1 to 23.5	y = 1.04x - 0.27	1.00	-0.48 to-0.05	1.02 to 1.05
2	50	10.8 to 16.5	y = 1.12x - 1.5*	0.98	-2.40 to -0.65	1.05 to 1.18
3	50	10.2 to 18.3	y = 1.05x - 0.59	0.98	-1.46 to 0.27	0.99 to 1.11
Total	224	5.1 to 23.5	y = 1.04x - 0.42	0.99	-0.62 to -0.22	1.03 to 1.06

Two sites met all the acceptance criteria except for study site 2, in which the Avie (venous) versus HiCN (venous) comparison had a slope slightly exceeding the 10% specification. Sponsor claimed that this was due to the relatively low number of samples at the extremes of the dynamic range. However, the combined data set across the three study sites met the specification (slope = 1.04), where the sample set (n = 224) includes samples at the extremes.

Summary of Data Point within ATE and LER Limits

	Fingerstick (FS) Avie vs. HemoCue	Venous Avie vs. HemoCue	Fingerstick (FS) Avie vs. HiCN	Venous Avie vs. HiCN
Min.	8.9	5.1	9.5	5.1
Max.	18.8	23.5	18	23.5
#Samples (5-13 g/dL)	52	67	45	67
#Samples (13.1-15 g/dL)	85	78	78	78
#Samples (15.1-24 g/dL)	47	79	54	79
Total Points	184	224	177	224
# Out Side ATE	8	30	0	0
%Within ATE	96	87*	100	100
%LER	0	0	0	0

All results were within the pre-specified ATE except for the results for Avie venous vs. Hemocue. However, a 100% ATE was achieved for Avie venous vs. HiCN venous, and HiCN is the recognized reference method. No points fell outside the LER limits for all comparative analyses.

b. Matrix comparison:

An internal matrix comparison study was conducted to establish the equivalency of fresh and frozen whole blood samples when tested on the Avie™ Total Hb Test System. Three whole blood samples, targeted at low, middle, and high levels of Hb (7 to 10 g/dL, 13 to 15 g/dL, and 20 to 22 g/dL, respectively) were tested (n=10) on the Avie™ system on the day of collection. Aliquots of each sample were prepared and stored frozen at -70°C overnight, and then re-assayed the next day with the same lot/serial number of materials. All observed absolute values of the t-statistic were at ≤0.5 within the pre-specified acceptance criteria and the data showed that there was no significant difference between fresh and frozen whole blood samples.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Reference range was established according to CLSI C28 A3 guidelines. Samples from 185 self-reported healthy individuals were collected and tested with the Avie test system. Of the 185 volunteers, there were 87 males and 98 females with age ranges between 18 and 87 years. No specific acceptance criteria were pre-established, as this was an observational study. The Hb results were sorted from low to high concentrations, and the 95% central interval for the Avie Total Hb Test System was identified to be 10.8 g/dL to 17.2 g/dL.

N. Instrument Name:

Avie™ Total Hb Reader

O. System Descriptions:

1. Modes of Operation:

   The test strips are single use and must be replaced in order to perform a new test.

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes __X__ or NO ____

3. Specimen Identification:

   There is no sample identification function with this device. Samples are applied directly to the test strip as they are collected.

4. Specimen Sampling and Handling:

   Fingerstick, capillary whole blood, or a drop of venous whole blood is directly applied from the finger or vial to the test strip. The test strip is then inserted into the reader.

5. Calibration:

   The Avie™ Total Hb reader is factory calibrated and is not user adjustable.

6. Quality Control:

   The Avie™ Total Hb reader has an internal control system that performs operational self checks (optics and software) when the device is turned on. If a malfunction is detected the reader will display an error message. The sponsor recommends that 3 levels of external controls be tested prior to running the first patient of the day, at least monthly if the device has not been used, every 3 months to check storage conditions, to become familiar with the testing process, to perform training or retraining of testing personnel, and whenever results do not match other clinical findings or symptoms.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Sample Volume:

Study was performed on three whole blood samples targeted at low, middle, and high levels of total Hb (approximately 7 to 9, 13 to 15, and 20 to 22 g/dL, respectively) to determine the effect of sample volume on the device. Each sample was tested in replicates (n = 5) at the following volumes: 1, 2, 3, 4, 5, and 6 µL. Averages of the replicate results were compared to the true value as determined by the in-house HiCN method. Based on the acceptance criteria of the on-test value and true value not greater than 10%, the results demonstrated that 3 µL is the minimum volume required for the Avie™ Total Hb Test system. The system is resistant to over-sampling, as the blood collection stops once the capillary is filled.

Qualification of In-house HiCN reference method:

The sponsor performed an in-house qualification study due to unavailability of commercial kits for the HiCN method, or reference laboratories that offer HiCN testing as a routine service. Studies were performed to qualify HiCN reference method that was used as the primary accuracy comparator for the Avie™ Total Hb Test System. Experiments to establish the limit of detection (LOD) and limit of quantitation (LOQ) were conducted according to CLSI EP17-A guide lines. For the in-house qualification study, inter-day precision was determined by calculating the %CV at each concentration evaluated and should be within 5% CV. Accuracy was determined by comparison of the measured results to the theoretical values and recovery was within 90% to 110%. Based on the data generated, the MEC HiCN in-house method was qualified for use.

Disinfection studies:

The device is intended for point-of-care use. The sponsor claimed that the Avie^{TM} Total Hb reader is same as Avie A1C reader (k093548) i.e. same foot print, same on-off switch, same location for strip or/cartridge insertion, and most importantly, the same external plastic materials are used, therefore allowing the disinfection studies data for Avie A1C to apply to Avie^{TM} Total Hb reader. Sponsor has provided the cleaning and disinfection studies that were performed on the Avie A1C meter by an outside commercial testing service to determine the robustness of the meter to the recommended cleaning and disinfection protocol, and its effectiveness in preventing the spread of blood borne pathogens, particularly hepatitis B virus (HBV). Fresh 10% bleach solution (EPA Reg. No: 5813-50) were validated, demonstrating complete inactivation of live virus for use with the meter. The sponsor also demonstrated that there was no change in performance or in the external materials of the meter after 650 disinfection and 650 cleaning cycles designed to simulate 3 years of healthcare professional use.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.